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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MOHAMED, ABDEL A	
ART UNIT	PAPER NUMBER
1654	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/19/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/823,819	FLEISZIG ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *12-19,21 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/2/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

ACKNOWLEDGMENT OF IDS, RESPONSE TO RESTRICTION REQUIREMENT AND STATUS OF THE CLAIMS

1. The Information Disclosure Statements (IDS) and Form PTO-1449 filed 02/02/05 and the response to the restriction requirement filed 09/21/06, respectively are acknowledged, entered and considered. Claims 1-22 are present for examination.

ELECTION WITH TRAVERSE

2. Applicant's election with traverse of Group I (claims 1-11 and 20) in the communication filed 09/21/06 is acknowledged. The traversal is on the ground(s) that the inventions of Groups I-III as disclosed and claimed in this application would most efficiently examined together because the inventions are not independent or distinct as claimed and there is no serious burden on the Examiner because a search for art related to methods of treating an ocular disease with a collectin would uncover art related to antimicrobial lenses. Accordingly, Applicant contends that it is proper to examine Groups I-III as one group for further prosecution is noted.

Contrary to Applicant's contention, Group I (claims 1-11 and 20) is drawn to a method for treating an ocular disease by administering collectin and/or surfactant protein, Group II (claims 12-15, 19 and 21) is drawn to ophthalmic composition comprising a collectin and/or surfactant protein and a kit formulation thereof, and Group III (claims 16-18 and 22) is drawn to an antimicrobial lens comprising a collectin and/or surfactant protein. Thus, the inventions as grouped are classified in different classes

and subclasses, and as such they are independent and distinct inventions, which differ in material make up, and formulations requiring different reaction condition and effect. Hence, one does not require the other for ultimate use and as such is capable of separate manufacture, use and sale, and is novel and patentable over each other.

Therefore, claims 12-19, 21 and 22 (Groups II and III) are withdrawn as non-elected inventions for the reasons of record. Hence, the Office action is directed to the merits of claims 1-11 and as *per* elected invention and Applicant is advised to cancel non-elected invention of claims 12-19, 21 and 22 in the next communication.

The requirement is still deemed proper and is therefore made FINAL.

OBJECTION TO TRADEMARKS AND THEIR USE

3. The use of the trademarks "Survanta®", "Alveofact®", "Infasurf®", and "Curosurf®" have been noted in this application. The trademarks have not been capitalized, they should be capitalized wherever they appear and be accompanied by the generic terminology. Although, the use of trademarks are permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in a manner, which might adversely affect their validity as trademarks.

Further, the specification, which specifies the generic terminology should include, published product information sufficient to show that the generic terminology or the generic description are inherent in the article referred by the trademarks. These

description requirements are made because the nature and composition of articles denoted by trademarks can change and affect the adequacy of the disclosure.

CLAIMS REJECTION-35 U.S.C. 112 1st PARAGRAPH.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11 and 20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of preparing an ophthalmic composition comprising a collectin and/or surfactant proteins in a kit and in antimicrobial lens formulation thereof, does not reasonably provide enablement for a method of treating an ocular disease such as dry eye or keratitis caused by a microbe encompassing bacterial, viral, fungal or protozoan pathogens in a subject by administering into the eye of a subject a pharmaceutical composition comprising a therapeutically effective amount of collectin and/or surfactant proteins in the manner claimed in claims 1-11 and 20. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with claims 1-11 and 20.

The instant specification teaches the method for preparing an ophthalmic composition comprising a collectin and/or surfactant proteins in a kit and in antimicrobial lens formulation thereof. Example 1 teaches the preparation of inocula by using strains of *Pseudomonas aeruginosa*, Example 2 discloses the collections of tears from human subjects, Example 3 shows the culturing of rabbit corneal epithelial cells, Examples 4 and 5 teach bacterial growth assays and bacterial invasion assays, respectively, Examples 7 and 8 are directed to ELISA for quantification surfactant protein D (SP-D) in tears and adsorption of SP-D from human tear fluid with Mannan-Sepharose. Similarly, Figures 1-7 disclose various *in vitro* assays, which show quantifications of bacterial invasion such as *P. aeruginosa* in corneal epithelial cells using collectin and/or surfactant proteins. The only *in vivo* experiment conducted is on Example 6 which discloses *in vivo* model of corneal infection to mice, wherein after anesthesia, three linear scratches were allowed to heal and the mice infected with bacteria and 14 days post-bacterial challenge, corneal disease was scored using two different grading system. Although, there is disclosure for *in vivo* experiment as discussed above in Example 6, however, there is no disclosure for a method of treating an ocular disease such as dry eye or keratitis caused by a microbe encompassing bacterial, viral, fungal or protozoan pathogens in a subject by administering into the eye of a subject a pharmaceutical composition

comprising a therapeutically effective amount of collectin and/or surfactant proteins in the manner claimed in claims 1-11 and 20.

Thus, there is no evidence in the instant specification to employ or administer the pharmaceutical composition useful for treatment of all kinds of ocular diseases in a subject as claimed, except for the mere recitation of protocols on pages 19-29 in the instant specification disclosing methods of administering a collectin and/or surfactant proteins to the eye to treat all kinds of ocular diseases in as subject without presenting any data or evidence to substantiate the protocols. Hence, the only support for the claimed method of treatment using the pharmaceutical composition in the specification is Applicant's supposition of the invention as recited in the protocols.

Further, the term "ocular disease" encompasses any disease of the eye and/or lacriminal system which includes the various disease conditions or situations listed on paragraph 0024 in the instant specification such as infectious and non-infectious blepharitus, hordeolum, diseases of the conjunctiva and sclerosis, diseases of the cornea, diseases of the uvea, etc. Thus, when these situations or disease conditions are added, undue experimentation would be required to determine which of the diseases conditions or situations would be treated by using the collectin and/or surfactant proteins in the manner claimed. Furthermore, Applicant's claims are directed to a very large number of diseases caused by a microbe which encompasses all kinds of bacteria, viral, fungal or protozoan pathogens by using specific pharmaceutical composition to treat any ocular disease, and there is no objective factual evidence in the

specification showing that treatment has occurred using the specific pharmaceutical composition claimed. Thus, one cannot employ or use or administer specific pharmaceutical composition in all situations without appropriate testing.

Moreover, on paragraph 0023, the instant specification defines the term "treating" as any indicia of success in the treatment or amelioration or prevention of an ocular disease, including any objective or subjective parameter such as abatement; remission; diminishing of symptoms or making the disease condition more tolerable to the patient; showing in the rate of degeneration or decline; or making the final point of degeneration less debilitating. Also, the term "therapeutic effect" is defined as the reduction, elimination, or prevention of the disease, symptoms of the disease, or side effects of the disease in a subject. While on paragraph 0024, as discussed above "ocular disease" encompasses any disease of the eye and/or lacriminal system which includes the various disease conditions or situations listed on paragraph 0024 in the instant specification such as infectious and non-infectious blepharitus, hordeolum, diseases of the conjunctiva and sclerosis, diseases of the cornea, diseases of the uvea, etc.

Furthermore, the reference of J. Wayne Streilein (Progress in Retinal and Eye Research, Vol. 18, No. 3, pp. 357-370, 1999) on page 363, under Importance of Immune Privilege in Ocular Diseases states that a large body of experimental and clinical evidence now indicates that immune privilege, as defined experimentally, is a critically important dimension to the ability of the immune system to provide protection for the eye. For example, there are times when immune privilege fails, and ocular disease ensues. Two experimental examples, model systems explored in mice,

illustrate this point, experimental autoimmune uveitis (EAU), and herpes stromal keratitis. On page 364, left column, third paragraph, the reference continues by stating that these findings emphasize two important points: first, immune privilege is a powerful mechanism for regulating systemic and local immunity within the eye; second, regulation of immunity in the eye may have deleterious consequences for the eye and for the host. In other words, immune privilege can be both a blessing and a bane.

Further, on page 368, under Rationale of Immune Privilege in the Eye, the reference states that over the past 20 years, investigators in ocular immunity privilege have gradually come to realize that immunity in the aye is a "two-edged sword". In general these mechanisms, though effective, are inflammatory and destructive, even of the innocent host tissues. The reference concludes on page 368 by stating that some of the important cellular and molecular features responsible for regulation of ocular immunity and privilege have been elucidated. But much remain to be done. First, we need to learn how the genes responsible for creating and maintaining ocular immune privilege are activated, expressed and regulated. Second, we need to understand how ocular immunity interacts with the systemic immune response, and how one influences the other. Third, the lessons learned from these studies should yield novel therapeutic approaches (gene therapy, molecular replacement therapy) that will have a salutary effect on many eye diseases with significant immune and inflammatory dimensions, ranging from acute and chronic uveitis, to macular degeneration and autoimmune diseases associated with viral infections. Thus, the reference clearly discloses immunoregulatory mechanism of the eye in which immunity to protect the eye from

invading pathogens is an absolute requirement for the preservation of vision (i.e., regulation of expression of immunity in the eye is critical to preservation of vision).

Therefore, in view of the above, the scope of the instantly claimed invention are very broad and speculative in that there is no working example or data or evidence which shows that the claimed compounds (i.e. collectin and/or surfactant proteins) are useful as a pharmaceutical compositions to treat ocular diseases such as dry eye or keratitis as claimed in claims 1-11 and 20. It would include those that have not been shown or taught to be useful or enabled by the disclosed method of making and using the invention. Moreover, undue experimentation is necessary to determine if and under what conditions, the claimed invention as broadly claimed is enabled, since a vast range of microbial populations in all kinds of possible treatment of ocular diseases by administering collectin and/or surfactant proteins are contemplated and are encompassed as well as wide range of situations. The results desired appear to be highly dependent on all variables, the relationship of which is not clearly disclosed. Hence, one of ordinary skill in the art would not be able to identify all the ocular disease treatments caused with wide range of pathogenic microbes intended to be effective for the claimed purpose as encompassed in the claims would be effective and under what conditions.

Further, the first paragraph of 35 U.S.C. 112 requires, *inter alia,* that a patent specification provide sufficient guidance to enable a person skilled in the art to make and use the claimed invention without undue experimentation. *In re Vaeck*, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991). While patent Applicants are not

directed to disclose every species that falls within a generic claim, *id.* at 496, 20 USPQ2d at 1445, it is well settled that "the scope of the claims must bear a reasonable correlation to the scope of the enablement provided by the specification". *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Where practice of the full scope of the claims would require experimentation; factors to be considered in determining whether a disclosure would require undue experimentation ..... include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *In re Wands*, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Therefore, applying the *Wands* factors to the facts of this case, one of skill in the art would find that undue amount of experimentation would be required to practice the full scope of the extremely broad claims fro the reasons given above. Thus, in view of the quantity of experimentation necessary, the lack of adequate guidance or working examples or data, and the breadth of the claims, the claims are not commensurate in scope with the enabling disclosure. Accordingly, filing of evidence commensurate with the scope of the claims or amendment of the claims to what is supported by the enabling disclosure is suggested.

CITATION OF RELEVANT PRIOR ART

5. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure: Fleiszig et al (Infection and Immunity, Vol. 71, No. 7, pp. 3866-3874, July 2003) disclose the use of whole human tear fluid for protecting corneal epithelial cells against *P. aeruginosa* virulence mechanism (i.e., against bacterium-induced cytotoxicity and inhibition of cellular invasion of the bacterial).

Ni et al (Infection and Immunity, Vol. 73, No. 4, pp. 2147-2156, April 2005) show that surfactant protein D (collectin) is present in human tear fluid and the cornea and inhibits epithelial cell invasion by *P. aeruginosa*.

CONCLUSION AND FUTURE CORRESPONDANCE

6. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272 0955. The examiner can normally be reached on First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tsang Cecilia can be reached on (571) 272 0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JON WEBER
SUPERVISORY PATENT EXAMINER

AM Mohamed/AAM
December 7, 2006